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A single-center outcome of choosing catheter ablation as the initial treatment in tachycardia–bradycardia syndrome and a new predictive factor for pacemaker implantation

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Abstract

Background The relationship between sinus node dysfunction and atrial fibrillation (AF) has been well known. The reversibility of sinus node dysfunction is indeed a critical factor in determining the treatment strategy in patients with tachycardia–bradycardia syndrome (TBS). We aimed to assess the clinical outcome of choosing catheter ablation as the initial treatment in tachycardia–bradycardia syndrome and predictive factors leading to the implantation of a permanent pacemaker (PPM) in these patients.

Methods Patients with TBS who had been taken AF catheter ablation from 2012 to 2021 were reviewed, and 113 patients were enrolled. Patients were divided into two groups based on whether a "sinus pause episode of more than 3 s unrelated to tachyarrhythmia" coexists (Group I, $n=20$) or not (Group II, $n=93$).

Results Compared to Group II, baseline characteristics showed that Group I was comprised of more female gender ($p=0.043$), with hypertension ($p=0.033$), and with enlarged left atrium ($p=0.003$). An average three-year follow-up found that eight patients (8/113, 7%) were implanted PPM (5/20, 25% in Group I vs. 3/93, 3.2% in Group II, $p=0.001$). Using a multivariate model, a "sinus pause episode unrelated to tachyarrhythmia" was strongly associated with PPM implantation after catheter ablation in patients with TBS (HR 6.765, 95% CI 1.355–33.763, $p=0.020$). Only four out of 113 patients (3.5%) progressed to persistent or permanent AF.

Conclusions After catheter ablation as the initial treatment in TBS, only 7% underwent PPM implantation, and an isolated sinus pause was a predictive factor for requiring PPM implantation. In addition, even in patients who undergo catheter ablation with subsequent PPM implantation, we can expect to improve the clinical outcome associated with a reduced AF burden.

Keywords Atrial fibrillation, Catheter ablation, Tachycardia–bradycardia syndrome, Sinus node dysfunction, Pacemaker

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Background

Atrial fibrillation (AF) and sino-atrial (SA) node disease frequently coexist [1], and efforts have been made to demonstrate which comes first. If the SA node is damaged for any reason, multiple ectopic atrial foci can occur as a lower pacemaker, which can lead to AF. From the opposite perspective, AF can promote overdriving suppression of the SA node, potentially resulting in prolonged pauses after AF termination [2]. Additionally, as the duration of AF becomes longer, the SA node undergoes electrical and structural remodeling, which can lead to irreversible damage [3, 4].

Reversibility of SA node dysfunction is very important in determining the treatment strategy in patients with tachycardia–bradycardia syndrome (TBS). Many studies have demonstrated that prolonged pauses after AF can be eliminated or the burden of both diseases reduced following catheter ablation of AF [5–7]. However, the latest guidelines for AF management recommend considering catheter ablation in patients with TBS because there is currently no strong evidence [8].

In the present study, we retrospectively evaluated a new predictive factor related to the requirement of a permanent pacemaker. Another aim of this study was to evaluate whether catheter ablation is a better treatment option for patients with TBS.

Methods

Study population

Between January 2012 and March 2021, we identified 255 consecutive patients with documented sinus pause episodes following the termination of AF and conducted an analysis on 113 of them. Exclusion criteria included patients who had received a permanent pacemaker (PPM) before catheter ablation, those who had undergone a maze procedure, totally thoracoscopic ablation, or those who were follow-up loss.

TBS was defined as a prolonged sinus pause (>3.0 s) after termination of AF with or without antiarrhythmic drugs (AADs) [9]. Bradycardia-related events were detected by 24 h-Holter monitoring before and after the ablation procedure in patients who had episodes of dizziness, presyncope, or syncope. These patients were divided into two groups based on whether a "sinus pause episode unrelated to tachyarrhythmia (isolated sinus pause)" coexists (Group I) or not (Group II) (Fig. 1). We

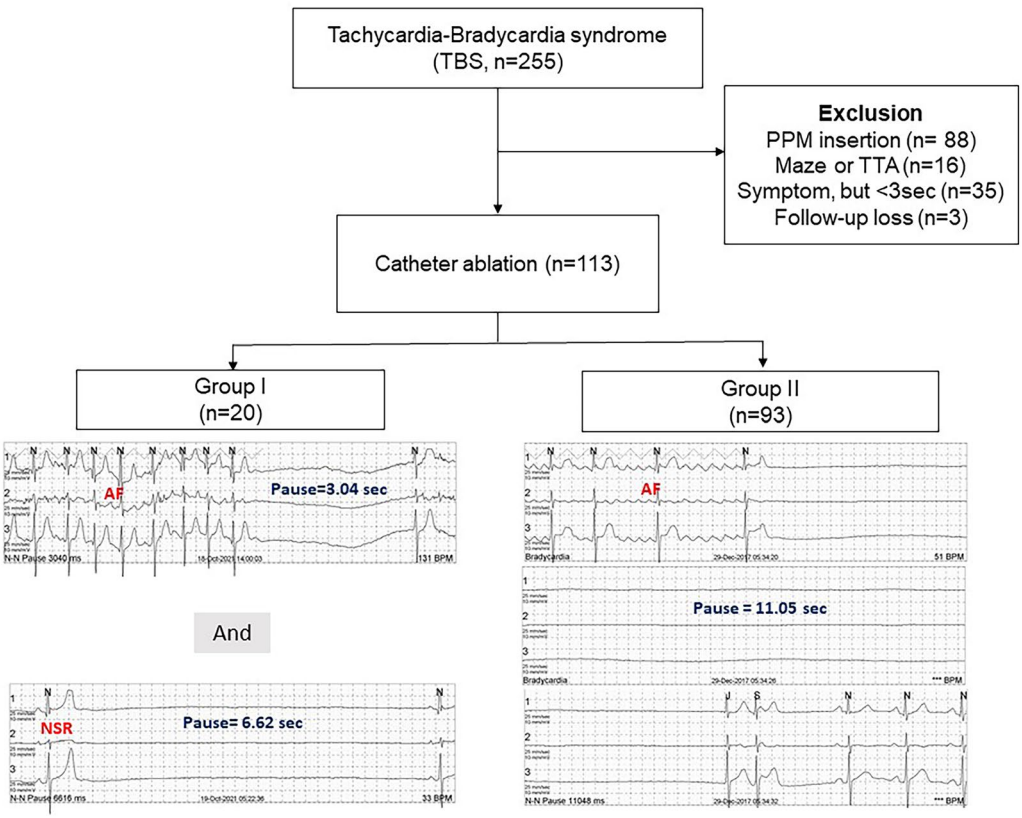

Fig. 1 Enrollment and flowchart of the study. *PPM* permanent pacemaker, *TTA* totally thoracoscopic ablation, *TBS* tachycardia–bradycardia syndrome, *AF* atrial fibrillation, *NSR* normal sinus rhythm

implanted PPM in case of severe bradycardia, isolated sinus pauses (> 3 s), or chronotropic incompetence following catheter ablation. The Samsung Medical Center Institutional Review Board (IRB) approved the study protocol and waived the need for consent from patients or relatives (IRB No. 2021–12-097–001).

Evaluation of Sinus node function

All patients discontinued antiarrhythmic drugs and the baseline heart rate was measured during admission day before catheter ablation. Sinus node recovery time (SNRT) was analyzed during a basic electrophysiologic study. SNRT was assessed by 30 s burst pacing at every 50 ms from 600 to 300 ms, which is determined as the longest time from the stimulus to the earliest SA node activity. The corrected SNRT was corrected based on the underlying sinus cycle length.

Procedure and follow-up

We selected RFCA (radiofrequency catheter ablation) or Cryoablation in physician preference at the first ablation, and acute success of pulmonary vein (PV) isolation was achieved in all patients. Redo-ablation was only performed by RFCA. All patients underwent continuous telemetry monitoring from before the catheter ablation procedure to 1 to 3 days afterward. The first outpatient clinic visit took place four weeks following the procedure. The patients were then scheduled for follow-up appointments every three to six months, which included a clinical interview, electrocardiogram, and/or 24-h Holter monitoring. Especially, patients with symptoms related to tachy- or bradyarrhythmia without evidence on electrocardiogram underwent Holter monitoring. AF recurrence was evaluated based on symptoms and defined as documented AF lasting longer than 30 s after three months. PPM implantation was considered when a patient experienced bradyarrhythmia-related symptoms such as dizziness, presyncope, or syncope, with a documented, prolonged pause lasting more than 3.0 s following catheter ablation.

Statistical analysis

Baseline data are presented as frequencies, mean ± standard deviation (SD), or median with interquartile range (IQR). Categorical variables were compared using $\chi 2$ tests or Fisher's exact tests. Comparisons of continuous variables in the same patients were performed using the paired t-test or Wilcoxon signed-rank test when appropriate. Continuous variables between the two groups were compared using the Student's t-test or Mann–Whitney test. COX regression analysis was performed to predict PPM implantation. A p-value < 0.05 was considered to be statistically significant. All statistical analyses were performed using IBM SPSS Statistics Software Version 27.0 (IBM, Armonk, NY, USA).

Results

Baseline characteristics

113 TBS patients who underwent catheter ablation as the first treatment for tachyarrhythmia were evaluated, and baseline data are summarized in Table 1. The clinical characteristics in both groups are comparable except for a higher prevalence of female gender (55% vs. 31.2%, $p = 0.043$), hypertension (60% vs. 34.4%, $p = 0.033$),

Table 1 Baseline characteristics

Factor	Group I ($n = 20$)	Group II ($n = 93$)	p-value
Age (years)	61.1 ± 57.3	57.3 ± 9.2	0.097
Female (n, %)	11 (55)	29 (31.2)	0.043
BMI (kg/m^2)	25.7 ± 3.5	24.5 ± 2.8	0.087
Longest pause (seconds)	5.9 ± 1.9	5.3 ± 2.0	0.220
CSNRT (msec)	595.6 ± 457.8	411.5 ± 370.2	0.141
Symptom (n, %)			
Dizziness	15 (75.0)	72 (77.4)	0.816
Presyncope	3 (15.0)	15 (16.1)	0.900
Syncope	2 (10.0)	30 (32.3)	0.045
Palpitations	15 (75.0)	60 (64.5)	0.368
Hypertension (n, %)	12 (60.0)	32 (34.4)	0.033
Diabetes (n, %)	4 (20.0)	12 (12.9)	0.409
Stroke/TIA (n, %)	2 (10.0)	12 (12.9)	0.721
PCI history (n, %)	1 (5.0)	3 (3.2)	0.697
CHAD2DS2-VASc score	2.0 ± 1.3	1.4 ± 1.3	0.054
Echocardiographic parameters			
LVEF (%)	63.3 ± 5.6	61.6 ± 5.4	0.214
LA diameter (mm)	45.0 ± 5.2	39.7 ± 7.2	0.003
E/E'	10.1 ± 3.0	8.8 ± 3.5	0.144
Anti-arrhythmic drugs before the procedure (n, %)			0.285
No medication	14 (70.0)	47 (50.5)	
Class Ic	4 (20.0)	31 (33.3)	
Class III	2 (10.0)	15 (16.1)	
Catheter ablation type (n, %)			0.940
RFCA	15 (75.0)	69 (74.2)	
Cryoablation	5 (25.0)	24 (25.8)	
AF duration (months)	27.4 ± 27.1	28.7 ± 37.1	0.884
Baseline heart rate (bpm)	65 ± 19	65 ± 14	0.929
Follow-up (months)	33.2 ± 36.6	36.8 ± 29.2	0.636

BMI body mass index, *TIA* transient ischemic attack, *LVEF* left ventricular ejection fraction, *LA* left atrium, *RFCA* radiofrequency catheter ablation, *AF* atrial fibrillation, *PCI* percutaneous coronary intervention, *CSNRT* corrected sinus node recovery time

and left atrium (LA) diameter (45.0 ± 5.2 vs. 39.7 ± 7.2, $p = 0.003$) in Group I. The longest pause and corrected SNRT show a numerical difference between the two groups, though without statistical significance (Group I vs. Group II, longest pause: 5.9 ± 1.9 vs. 5.3 ± 2.0 s, corrected SNRT; 595.6 ± 457.8 vs. 411.5 ± 370.2 ms). Patients in Group I and Group II underwent follow-up for a mean of 33.2 ± 36.6 months and 36.8 ± 29.2 months, respectively ($p = 0.636$).

Permanent pacemaker implantation

Only 7% (8/113) of the patients required a PPM after catheter ablation. A higher percentage of patients in Group I received a PPM implantation compared to Group II (25% vs. 3.2%, $p = 0.001$), as shown in Fig. 2.

Sixteen percent of patients (16%, 18/113) demonstrated a significantly prolonged sinus pause (> 3 s) following catheter ablation, and eight of 18 patients who finally received an implanted pacemaker had a prolonged pause with significant bradyarrhythmia-related symptoms. The details of the eight patients who received PPM implantation are summarized in Table 2. The reason for PPM implantation was that 50% of the patients (4/8) experienced a significantly prolonged pause with symptoms during their inpatient stay for catheter ablation. One patient (no. 4) received a PPM implantation because TBS recurred despite undergoing a re-RFCA procedure.

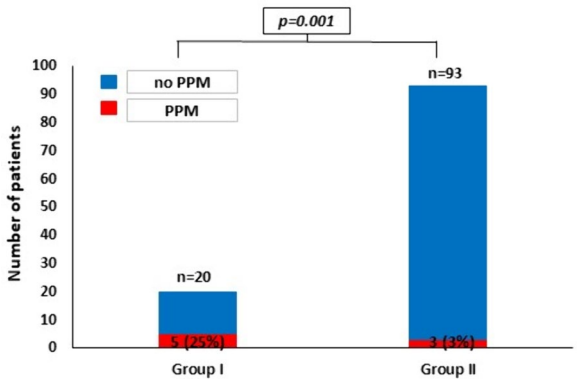

Fig. 2 Comparison in rate of permanent pacemaker implantation. *PPM* permanent pacemaker

The presence of a "Sinus pause episode unrelated to tachyarrhythmia" was associated with PPM implantation using both univariate analysis (HR 6.784, 95% CI 1.039–44.310, $p = 0.046$) and multivariate models (HR 6.765, 95% CI 1.355–33.763, $p = 0.020$), with adjustments for sex, age, Hypertension, LA diameter, left ventricular ejection fraction, corrected SNRT and longest pause before RFCA (Table 3).

Comparison of clinical outcomes ± pacemaker implantation

Recurrence of AF in PPM patients and no PPM patients occurred in 37.5% (three of eight) and 28.6% (30 of 105), respectively. Sixteen patients needed to undergo additional catheter ablation for AF recurrence, and one of 16 patients presented prolonged pauses that required device implantation despite redo-RFCA. Maintenance of sinus rhythm (SR) without AAD medication for longer than 12 months (12 months AADs off SR) was higher in no PPM than in PPM Patients (58/105, 55.2% vs. 1/8, 12.5% $p = 0.020$). Only four patients progressed to persistent or permanent AF. Rhythm outcomes are summarized in Table 4.

Discussion

Our data showed that over a 3-year follow-up period, only 7% (8/113) of the patients with TBS required a PPM after catheter ablation and the presence of "sinus pause episodes unrelated to tachyarrhythmia" is a predictive factor in determining the PPM implantation in patients with TBS. Group I and II had comparable longest sinus

Table 2 The information of the eight patients who received a pacemaker implantation

Patients no	Sex/age	Group	Documented longest pause (s) (following ablation)	Symptom(s)	redo-RFCA	Time interval from CA to PPM	Last follow-up	
							ECG	AAD
1	M/54	I	10.4	Dyspnea and dizziness	No	5 days	RSR	Yes
2	M/59	I	6.4	Dizziness	No	2 days	RSR	Yes
3	F/56	II	7.3	Dizziness	No	3 days	A pacing rhythm	Yes
4	F/39	II	5.4	Syncope	Yes	26 months	RSR	Yes
5	M/58	I	4.04	Syncope	No	63 months	RSR	Yes
6	M/60	II	4.59	Dizziness	No	5 months	RSR	Yes
7	F/80	I	7.43	Presyncope	No	3 days	A pacing rhythm	Yes
8	F/73	I	3.1	Syncope	No	6 months	RSR	No

CA catheter ablation, *RFCA* radiofrequency catheter ablation, *PPM* permanent pacemaker, *AAD* anti-arrhythmic drug, *RSR* regular sinus rhythm, *ECG* Electrocardiogram

Table 3 Predictors of pacemaker implantation following ablation

Factors	HR (univariate analysis)	*p*-value	HR (multivariate analysis)	*p*-value
Female	1.482 (0.242–9.085)	0.671		
Age	0.953 (0.836–1.085)	0.466		
Hypertension	2.629 (0.302–22.869)	0.381		
LA diameter	0.997 (0.854–1.165)	0.972		
LVEF (%)	0.828 (0.675–1.016)	0.071		
cSNRT	1.001 (0.999–1.003)	0.577		
Sinus pause episode unrelated to tachyarrhythmia	6.784 (1.039–44.310)	0.046	6.765 (1.355–33.763)	0.020
Longest pause before CA	1.213 (0.835–1.763)	0.311		

Values are expressed as hazard ratio (HR) with CI 95%

LVEF left ventricular ejection fraction, *LA* left atrium, *AF* atrial fibrillation, *CA* catheter ablation, *SND* sinus node dysfunction, *cSNRT* corrected sinus node recovery time

Table 4 Rhythm outcomes over a three-year follow-up period

	PPM ($n=8$)	No PPM ($n=105$)	*p*-value
Baseline heart rate (bpm)	58 ± 15	66 ± 15	0.159
> 3 s Pause after CA ablation	8 (100)	10 (9.5)	< 0.001
Recurrence of AF	3 (37.5)	30 (28.6)	0.592
Redo/Trido-RFCA	1 (12.5)	15 (14.3)	0.889
Rhythm outcome at last FU			0.001
Sinus rhythm	5 (62.5)	97 (92.4)	
Paroxysmal AF	3 (37.5)	4 (3.8)	
Persistent/permanent AF	0 (0.0)	4 (3.8)	
12-month AAD Off NSR	1 (12.5)	58 (55.2)	0.020

CA catheter ablation, *RFCA* radiofrequency catheter ablation, *PPM* permanent pacemaker, *AF* atrial fibrillation, *AAD* anti-arrhythmic drug, *NSR* normal sinus rhythm, *FU* follow-up

pause durations; however, there was a higher prevalence of female gender, hypertension, and LA diameter in Group I.

SA node disease can result from extrinsic factors or be caused by intrinsic changes of the SA node itself [10]. Extrinsic causes of SA node disease include electrolyte imbalance, hypothyroidism, excessive vagal tone, and pharmacologic agents including antiarrhythmic drugs. Several experimental studies have suggested that adenosine can affect SA node function after termination of AF [11, 12]. Unlike correctable extrinsic factors, intrinsic SA node disease is characterized by irreversible fibrotic tissue changes [13]. "Sinus pause episodes unrelated to tachyarrhythmia" in this study indicates potentially SA node fibrosis, suggesting the possibility of a chronic state of SA node disease.

There is a bidirectional relationship between brady- and tachyarrhythmia [1], but it is unclear which occurs first. Chen et al. suggested that a well-conditioned connection between the SA node, atrial myocardium, and pulmonary veins is an important mechanism for preventing arrhythmia [14]. With this balance of pathophysiological conditions, the reversibility of SA node function is a crucial factor for predicting PPM implantation. Several clinical studies have shown that curative AF ablation can decrease sinus pauses after termination of AF [5, 15, 16]. In 89% (101/113) of patients, except for patients who progressed to persistent AF ($n=4$), even if AF recurred, AF burden decreased through additional RFCA, and patients did not require PPM implantation.

Despite efforts to reduce the burden of atrial tachyarrhythmia, it could not be completely free from the requirement of device implantation. Several studies presented a PPM implantation rate of 6.8% to 11.3% [6, 17–19]. Inada et al. showed that 8% (3/37) of patients needed PPM implantation due to the gradual progression of sinus node dysfunction or recurrence of TBS [6]. Hwang et al. implanted PPM in 11.3% (25/222) of patients, and half (14/25) required implantation within a three-month blanking period [19]. These results were consistent with the present study; a PPM was required after catheter ablation in only 7% (8/113) of TBS patients.

Beneficial clinical outcomes of catheter ablation (CA) for the treatment of TBS are well known. A previous study demonstrated that a higher proportion of patients in the PPM group progressed to persistent AF compared to the CA group (9.9% vs. 1.3%, $p<0.05$) over 10 years [20]. Cho et al. compared the PPM and CA groups for 3.5 years, and the CA group showed less progression to persistent AF than the PPM group (HR 0.2, CI 0.06–0.063, $p=0.006$) [21]. Consistent with these findings, in this study, only 4 patients (4/113, 3.5%) progressed to persistent/permanent AF.

The recent pacing guideline suggests that CA could be considered as an alternative to PPM implantation due to limited data in patients with AF-related bradycardia [22]. In several retrospective studies, there is a tendency for CA to be performed in selected patients, such as those

of younger age in comparison with the general compared with general pacemaker population (around 65 years vs. over 75 years) [6, 7, 23, 24]. In this study, with an average age of around 60 years, which is relatively consistent with other studies, there is a probability that selected patients may have favorable conditions for undergoing catheter ablation. Further studies are needed to elucidate the criteria for preferring catheter ablation over a pacemaker in these patients.

The present study had several limitations. Firstly, being a retrospective study conducted at a single center, there is a potential for bias and incomplete data. Secondly, we assessed brady- and tachyarrhythmia without continuous rhythm monitoring, which may have led to an underestimation of asymptomatic AF and the duration of pauses. Thirdly, there would be selection bias for catheter ablation, limiting the generalizability of our findings.

Conclusions

This study suggests that, over a 3-year follow-up period, only 7% of the patients with TBS required a PPM after AF catheter ablation, and "sinus pause episode unrelated to tachyarrhythmia" was associated with the need for implantation of PPM after catheter ablation. AF catheter ablation could be the initial treatment option that is expected to yield better clinical outcomes in these patients.

Abbreviations

AF	Atrial fibrillation
PPM	Permanent pacemaker
TBS	Tachycardia–bradycardia syndrome
SA	Sino-atrial
LA	Left atrium
AAD	Antiarrhythmic drug
SNRT	Sinus node recovery time
PV	Pulmonary vein
SD	Standard deviation
IQR	Interquartile range
SR	Sinus rhythm
HR	Hazard ratio
RFCA	Radiofrequency catheter ablation

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Author contributions

HR Kim and YK On were major contributors to analyzing data and writing the manuscript. JY Kim was involved in creating the concept of the study. J Kim, K Park, and SJ Park reviewed and revised the manuscript. All authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate

This study protocol was approved by the Institutional Review Board at Samsung Medical Center, which waived the requirement of obtaining written informed consent from patients.

Competing interests

The authors declare that they have no competing interests.

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